

US EPA ARCHIVE DOCUMENT

12-2-93

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MRID No. 419633-03

DATA EVALUATION RECORD

1. CHEMICAL: Acetochlor. Shaughnessey Number: 121601.
2. TEST MATERIAL: Acetochlor; Batch No. P2; 90.4% purity; a dark brown liquid.
3. STUDY TYPE: Avian Single Dose Oral LD₅₀ Test.
Species Tested: Bobwhite quail (*Colinus virginianus*).
4. CITATION: Hakin, B., A.J. Johnson, A. Anderson, J.G. Maxwell, and C.G. Howse. 1990. Acetochlor: Acute Oral Toxicity (LD₅₀) to Bobwhite Quail. Study performed by Huntingdon Research Centre Ltd, Cambridgeshire, England. Laboratory study No. ISN 235/90893. Submitted by ICI Agrochemicals, Surrey, England. MRID No. 419633-03.

5. REVIEWED BY:

William S. Rabert
Biologist
Ecological Effects Branch
Environmental Fate and Effects Division

Signature: *William S. Rabert*
Date: *10/20/93*
(7507C)

6. APPROVED BY:

Dan Rieder
Section Head
Ecological Effects Branch
Environmental Fate and Effects Division

Signature: *Dan Rieder*
Date: *11.9.93*
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Henry T. Craven, M.S.
Supervisor, EEB/EFED
USEPA

Signature: *H. T. Craven*
Date: *12/2/93*

7. CONCLUSIONS: The study is scientifically sound and meets the requirements for an avian LD₅₀ study. [Inverted mortalities at two test levels produced widely different LD₅₀'s, broad confidence limits, and low goodness of fit for the three statistical methods (i.e., LD₅₀ values were 49, 121 and 131 mg/kg for the binomial, moving average and probit method, respectively). The most conservative LD₅₀ value of 49 mg/kg was selected as the endpoint for this study. This classifies the test substance as highly toxic to bobwhite quail.] The NOEC was 8 mg/kg.

8. RECOMMENDATIONS: N/A

9. BACKGROUND:

10. DISCUSSION OF INDIVIDUAL TESTS: N/A.

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11. MATERIALS AND METHODS:

- A. **Test Animals:** The birds used in the study were young adult bobwhite quail (*Colinus virginianus*) over 16 weeks of age. The birds were obtained from D.R. and R.E. Wise, Cambridgeshire, England. All birds were acclimated to the facilities for 14 days prior to dosing.
- B. **Test System:** All birds were housed indoors in pens constructed of polyethylene coated stainless steel wire. Pen dimensions were not specified in the report. Artificial lights provided 7 hours of light per day. Maximum and minimum temperatures and the relative humidity of the animal room were recorded once daily. The average temperature ranged from a minimum of $16^{\circ}\text{C} \pm 2.3^{\circ}\text{C}$ to a maximum of $21^{\circ}\text{C} \pm 2.1^{\circ}\text{C}$ (SD). The average relative humidity was $69\% \pm 7.9\%$ (SD).
- C. **Dosage:** 14-day single dose oral LD_{50} test. Based upon an initial range-finding study, nominal dosages selected for the study were 8, 31, 125, 500, and 2000 milligrams of acetochlor per kilogram of body weight (mg/kg). The dosages and reported LD_{50} value were not corrected for purity of the test substance. Analyses of the test formulations were conducted by Huntingdon Research Centre Ltd. to determine the concentration of acetochlor in dose preparations used in the study.
- D. **Design:** Groups of ten birds (five males and five females) were allocated to each of five treatment groups and one control group, so that all groups initially had similar mean bodyweights. Water was available at all times and food was offered ad libitum with the exception of an overnight starvation period of at least 21 hours prior to dosing. The birds were offered standard Huntingdon Research Centre layer diet in pellet form from Whitworth Brothers Ltd, Cambridgeshire, England. The test substance was administered in suspension in corn oil by oral intubation using a disposable syringe and a plastic catheter. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight. The control birds were given a corresponding volume of corn oil only.

Bird health and mortalities were observed daily throughout the study period. The birds were individually weighed during acclimation (days -14 and

-7) and on days 0, 7 and 14 of the test period. Group mean food consumption was determined weekly throughout the acclimation period and the study period.

Macroscopic post-mortem examinations, as well as histological examinations of kidney, heart, liver and lung, were performed on all birds.

E. **Statistics:** Due to the pattern of mortality, the LD₅₀ was not calculated.

12. **REPORTED RESULTS:** There were no mortalities in the control group or in the lowest dosage group (8 mg/kg). Mortalities of 40 to 80% were observed in the remaining four treatment groups (Table 1, attached).

All birds in the control group and the 8 mg/kg treatment group remained in good health throughout the study. Birds in the highest dosage group (2000 mg/kg) showed subdued behavior on days 1 and 2. Seven of the birds in this group died on day 1 and another died on day 2. Birds dosed at 31 mg/kg, 125 mg/kg, and 500 mg/kg showed clinical signs of toxicity beginning on day 4 and continuing until death. These signs included subdued behavior, unsteadiness of gait, ruffled feathers, weakness and inability to stand. One bird dosed at 125 mg/kg had a swelling on the back of its head on day 5.

During post-mortem examination, a colorless gelatinous substance was observed covering the breast and crop of two birds from the highest dosage group. Both birds died on day 1 after dosing. A white powdery deposit was observed in the body cavity of all birds which died on or after day 3 of the study. One or more of the following organs was affected: heart, liver, lungs, gizzard. No abnormalities were detected in any other birds.

Tissues from all birds were processed for histological examination. Prepared sections were sent to ICI Agrochemicals for evaluation. The results of these examinations were not reported in the study.

No apparent effects on body weight change were reported (Table 2, attached). During day 1 following dosing, food consumption by the one surviving male bird in the highest dosage group was very low prior to its death on day 2. The study revealed no other evidence of treatment-related effects on food consumption (Table 3, attached).

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:

The acute oral LD₅₀ of acetochlor could not be determined because of the spread of mortalities in treatment groups. Toxic effects were observed in birds at all dose levels except the 8 mg/kg group. At 8 mg/kg, no effects were observed on any of the parameters measured.

The report stated that the study was conducted in conformance with Good Laboratory Practice regulations. The "Good Laboratory Practice Compliance Statement" was signed by representatives of Huntingdon Research Center Ltd. and ICI Americas, Inc.

14. REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS:

- A. Test Procedure: The test procedures were in accordance with Subdivision E and SEP guidelines with the following exceptions:

The authors did not report an LD₅₀ value because of the non-dose related mortalities in test groups at two test concentrations. Mortalities of 70 and 60 percent were observed at 125 and 500 mg/kg, respectively. [The inverted mortalities at two test levels produced widely different LD₅₀'s with broad confidence limits for the three statistical analyses (i.e., LD₅₀ values were 49, 121 and 131 mg/kg for the binomial, moving average and probit method, respectively). Low goodness of fit was found for the probit method.] *added*

Pen size was not specified.

Birds were not randomly allocated to treatment groups, as stipulated by the SEP guidelines. Rather, birds were selected and allocated so that all groups had similar mean bodyweights at the study initiation.

[As consequence of these problems, the most conservative LD₅₀ value of 49 mg/kg was selected as the endpoint for this study.] The NOEC was 8 mg/kg.

- added*
B. Statistical Analysis: The reviewer calculated the LD₅₀ using EPA's Toxanal computer program (attached). Using the Binomial test, a LD₅₀ of 49 mg/kg was calculated. [Confidence limits were estimate to be 0 and infinity, because of the spread of mortalities in treatment *added* groups.] The Moving Average Method calculated a LD₅₀ of 122 mg/kg, with 95% confidence limits of 47 and 315 mg/kg. The LD₅₀ calculated by the Probit Method is 131 mg/kg with 95% confidence limits of 40 and 445 mg/kg.

- C. Discussion/Results: The study's most serious deviation from recommended guidelines is that the authors did not report a LD₅₀ value, due to the inverted distribution of deaths across test groups. [Results of the reviewer's analyses using EPA's toxanal program indicated that the Probit Method had a very low goodness of fit (i.e., 0.204) and hence is unacceptable. The LD₅₀ value of 49 mg/kg for the Bionomial Method was within the confidence limits of the other methods and hence was selected as a conservative estimate of the LD₅₀ value. Therefore, the study is scientifically sound and meets the requirements for an avian LD₅₀ study. The LD₅₀ of 49 mg/kg classifies the test substance as highly toxic to bobwhite quail.] *revised*
The NOEC was 8 mg/kg.

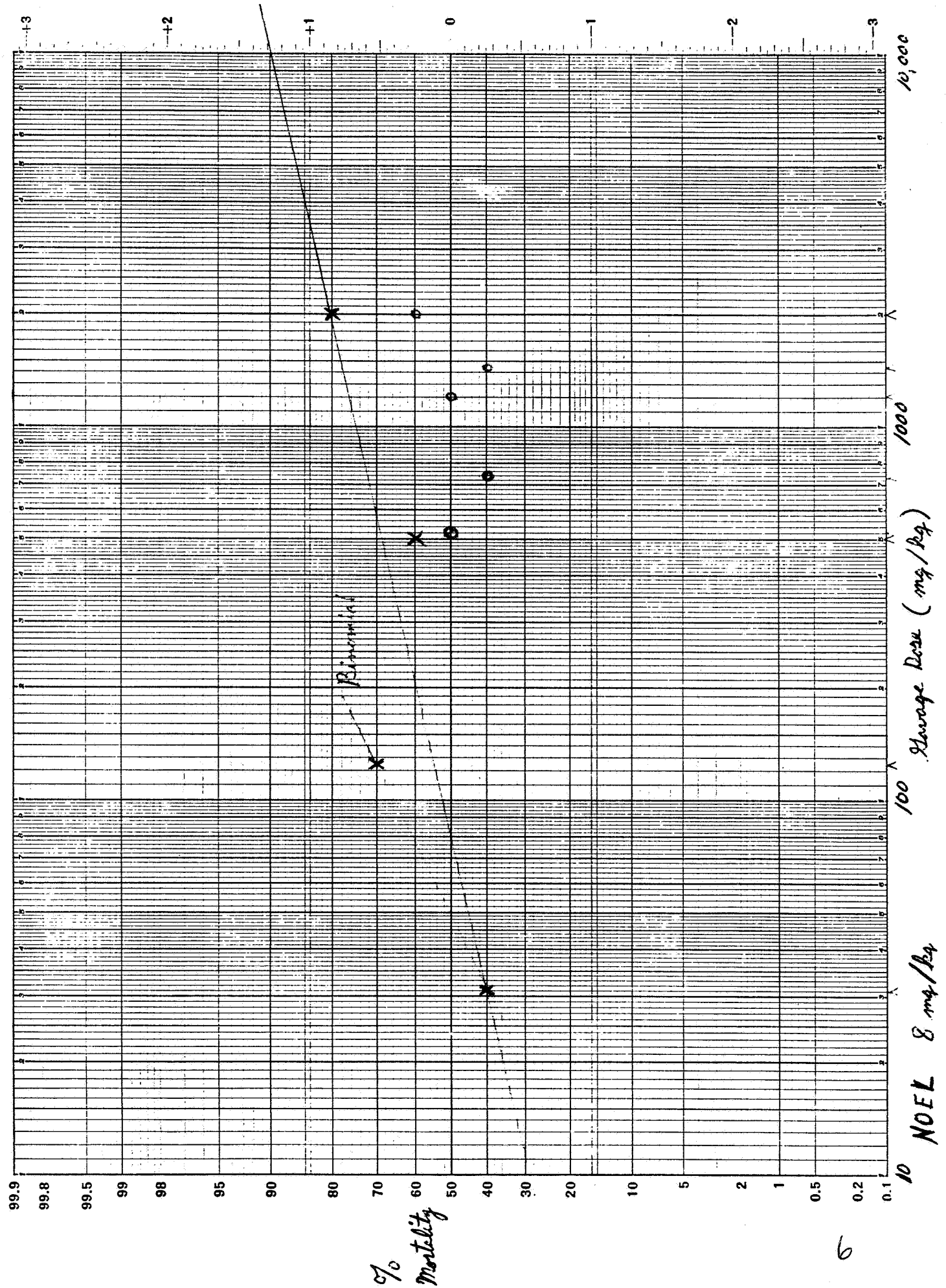
Although the authors concluded that there were no effects on body weight, Table 2 (attached) shows that the two surviving females in the 2000 mg/kg group lost considerable weight after dosing, especially from day 0 to day 7. The reviewer considers this to be treatment-related.

D. Adequacy of the Study:

- (1) Classification: Core.
- (2) Rationale: N/A.
- (3) Repairability: N/A.

15. COMPLETION OF ONE-LINER: Yes; October 21, 1993.

90.4% Acetochlor - Bobwhite Quail. LD50



DATA EVALUATION RECORD

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5. **REVIEWED BY:**

Carolyn F. Poppell, Sc.M.
Senior Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: *Michael L. Whitten*
for Carolyn Poppell
Date: 11/18/91
6. **APPROVED BY:**

Michael Whitten, M.S.
Wildlife Toxicologist
KBN Engineering and
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Signature: *Michael L. Whitten*
Date: 11/18/91

Henry T. Craven, M.S.
Supervisor, EEB/EFED
USEPA

Signature:
Date:
7. **CONCLUSIONS:** The study is scientifically sound and meets the requirements for an avian LD₅₀ study. The LD₅₀ of 131 mg/kg classifies the test substance as moderately toxic to bobwhite quail. The NOEC was 8 mg/kg. *Revised*
8. **RECOMMENDATIONS:** N/A
9. **BACKGROUND:**
10. **DISCUSSION OF INDIVIDUAL TESTS:** N/A.

ACETOCHLOR

Page is not included in this copy.

Pages 8 through 10 are not included.

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients.
 - ☐ Identity of product impurities.
 - ☐ Description of the product manufacturing process.
 - ☐ Description of quality control procedures.
 - ☐ Identity of the source of product ingredients.
 - ☐ Sales or other commercial/financial information.
 - ☐ A draft product label.
 - ☐ The product confidential statement of formula.
 - ☐ Information about a pending registration action.
 - ☒ FIFRA registration data.
 - ☐ The document is a duplicate of page(s) .
 - ☐ The document is not responsive to the request.
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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

CAROLYN POPPELL ACETOCHLOR BOBWHITE QUAIL 10-16-91

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
2000	10	8	80	5.46875
500	10	6	60.00001	37.69531
125	10	7	70	17.1875
31	10	4	40	37.69531
8	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 0 AND +INFINITY CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 49.0632

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS
4	.2148831	122.1425	46.67343 315.4559

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.3061772	1	.2043317

SLOPE = .8775314
95 PERCENT CONFIDENCE LIMITS = .3919645 AND 1.363098

LC50 = 131.3568
95 PERCENT CONFIDENCE LIMITS = 39.94159 AND 444.5479

LC10 = 4.690411
95 PERCENT CONFIDENCE LIMITS = 6.050535E-02 AND 19.75875
